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Clinical Studies of Styrene Workers: Initial Findings

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Styrene monomer is a high volume chemical used chiefly in production of polystyrene. A clinical survey of 493 production workers was undertaken at the oldest and largest monomer production, polymerization, and extrusion facility in the U.S. Relative exposure durations and levels were obtained from occupational histories. Significant differences between the high and low exposure groups were found with regard to history of acute prenarcotic symptoms, acute lower respiratory symptoms, prevalence of $FEV_1/FV < 75\%$, and elevated GCTP. Other liver function tests, chest x-ray, $FVC < 80\%$, and hematological parameters showed no distinct pattern. A concomitant mortality study has been mounted and is in progress.

About 2.8 million tons of styrene were produced in the United States in 1973, slightly less than toluene and slightly more than vinyl chloride (*1*). Polystyrene and styrene polymers (butadiene–styrene, acryonitritile–butadiene–styrene for example) production totaled 2.2 million tons in 1974 and was expected to rise to 11 millions tons by the year 2000 (*2*). The other major use of styrene is as a crosslinking agent in polyester resin manufacture; 30–40% of the volume of fresh resin may be styrene (*3*).

Physically, styrene monomer is a volatile liquid (see Table 1); most human exposure is to this form. During the commonly used hand layup glass fiber–polyester resin process, evaporation rates of styrene are on the order of 50 g/m² in 30 min; exposures are of the order of 100–200 ppm (*3–5*) time-weighted average (TWA) over a several hour period. Levels in styrene production or polymerization are less readily obtained. Barcotti (*6*) gave a level of 192 ppm during polymerization, 25–50 ppm for other tasks. In addition, heating commercial polystyrene may give off styrene in amounts up to several hundred to a few thousand parts per million (*7,8*).

The partition coefficient of styrene favors steady-state concentrations which are highest in fat and decrease progressively from fat to blood to water to air (*9,10*) (Table 1). Styrene has been found in the fat of occupationally exposed workers (*11*).

Table 1. Properties of styrene monomer.

Property	
Structure	$C_6H_5 - CH = CH_2$
Freezing point, °C	30.6
Boiling point, °C	145.2
Vapor pressure at 25°C, mm Hg	6.1
Air saturated with styrene at 25°C, ppm	8026
Vapor density	3.6
Explosive limits, ppm	11,000–61,000
Conversion factor	1 ppm = 4.2 mg/m³
Water solubility, mg/l.	
Miscible in common organic solvents	300
Partition coefficients:	
Water/air	4.38
Blood/air	32
Oil/blood	130
Oil/air	4160

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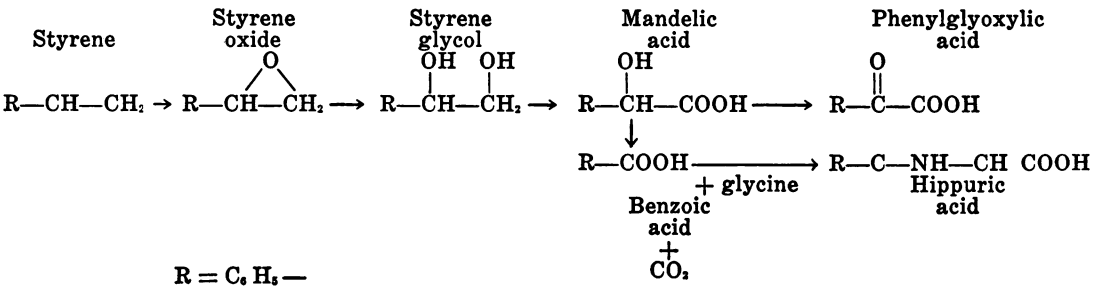
Dynamically, styrene is well absorbed through the lungs (about 70–90% of that contained in the alveolar ventilation) (*12,13*). Over a concentration range of 0–350 ppm and over a period of several hours, the same proportion of inspired styrene continues to be absorbed (*12*). Styrene is also well absorbed through the skin (*14*). Blood styrene continues to rise over time during this period (*13,15*).

Styrene is metabolized in man (about 1% expired unchanged) to a mixture of hippuric, phenylgloxylic, and mandelic acids (*16*) which are excreted in the urine. The primary metabolic pathway is outlined in eq. (1). Liebman (*17*) reviewed the pathway and summarized the evidence for styrene oxide being the first metabolic step.



(1)

Styrene oxide has been shown to be a base-substitution mutagen; other metabolites were not found to be mutagenic (*18*). The evidence for the mutagenicity of styrene itself is mostly negative (*18*); however, Vainio (*19*) has stated that styrene may be mutagenic in the presence of a microsomal system. It may be that styrene oxide is produced by microsomes.

The metabolism of styrene takes place in the liver; it is stimulated by phenobarbital and suppressed by coadministered toluene (*20*). At low level styrene exposure (1–50 ppm over few hours) an increase in mandelic acid excretion in the urine is detectable (*4,16,21–23*), peaking about 4–5 hr after a 1–2 hr exposure. At high level exposure of about 100 ppm TWA (*4, 16*), the excretion rate of the metabolites reaches a plateau. A significant increase in hippuric acid excretion occurs (*16,24*), an observation first noted for high exposure in 1944 (*24*). This peak of hippuric acid excretion rate is delayed for about 20 hr (*16*).

Toxicology

The toxic effects of styrene were first reported for acute and chronic exposures in 1942 (*25*). At exposures of 5000 ppm, most animals were unconscious within 1 hr and all died within 8 hr of apparent CNS depression. At exposures of 1300 ppm, a small proportion of rats and all guinea pigs died after 40 hr of continuous exposure of pulmonary edema. Acute liver and kidney damage were also noted. At 1300 ppm for 8 hr daily, 5 days per week for 6 months, 10% of guinea pigs died of pulmonary irritation within a few days. Slight increase in weight of liver and kidney was noted for rats. Eye and nose irritation was common at 1300 ppm and present at 650 ppm. Hematological values were not altered. Lifetime studies were not done. Gut (*26*) found that the spontaneous motor activity in the rat decreased at levels of several hundred ppm for 8 hr.

Studies in humans (see Table 2) have found related effects in acute experiments lasting a few hours at 800 ppm (*24*). The subjects were grossly unsteady and drowsy, with nasal and eye irritation and a metallic taste in the mouth. They felt tense and depressed. In the range of 350 ppm irritation was still strong, and objective tests of coordination and dexterity (*15*) and reaction time were abnormal. Gamberale (*27*) also found that subjects felt affected and tense after exposure. At a level of 200 ppm, Oltramare (*13*) found increased reaction times in 30%; Gamberale (*27*) found no change. Irritative symptoms were present to 50–100 ppm (*13,15*), reaction time increases and subjective symptoms were inconsistently present (*13,15, 27*). Odor was noted to levels of 3–5 ppm, but irritation, increased reaction time, and subjective symptoms (*13*) were absent. Acute pulmonary function changes, or acute liver function changes have not been systematically examined in human subjects.

Table 2. Toxic effects of styrene in humans.

Reference	Number examined	Process resin/rubber	Dose, ppm × yr	Effects
Barsotti, 1952 (*6*)	41	Monomer manufacture, polymerization	24–196 × years	Slight leucopenia, relative lymphocytosis, irritation, decreased night vision, urinary hippuric acid normal
Katz, 1962 (*33*)	526	Rubber	ca. 20 × years	Hepatomegaly (30%), splenomegaly (6%), increased bilirubin (30%), leucopenia (30%), reticulocytosis (59%)
Zielhuis, 1962 (*3*)	55	Resin	10–200, up to 5 yr	Hematology normal, differential normal, irritation, drowsiness
Pratt-Johnson, 1964 (*28*)	1	Resin	Unknown × 5 yr	Retrobulbar neuritis, reverting after one year, headache, sleepiness, dyspepsia
Huzel, 1967 (*5*)	55	Resin	50–100 × yr	Weltman reaction 48% Hematology normal
Benini, 1970 (*32*)	99	Rubber	Unknown	High red blood count, high siderocytes
Araki, 1971 (*29*)	1	Resin	Unknown × 14 yr	Peripheral neuropathy, EMG abnormal, EEG normal, hematology normal, liver normal, skin atrophy.
Gotell, 1972 (*4*)	12	Resin	100–200 × years	Increased reaction time, urine mandelic acid elevated
Klimokova-Deutskhova, 1973 (*30*)	105	Resin	Unknown × years	Headache, sleepiness, peripheral neuropathy, EMG, deteriorating EEG, nystagmus, facial palsy
Chemielewski, 1973 (*31*)	101	Resin	Unknown × years	Blood protein, lipid normal above average, glucose tolerance
Oltramare, 1974 (*13*)	5	Resin	20–560 × years	3/5 increased bilirubin, 2/5 wbc below 5000

Styrene effects have been most widely studied in the use of polyester resin to make laminates (glass fiber) or related processes (*3,5,13,28–31*). Some have studied copolymer production in synthetic rubber manufacture (*32–33*). A summary of a number of studies is given in Table 2. Studies of styrene manufacturing and polymerization factory were reported only by Barsotti (*6*) in 1952. He found irritation, especially of skin and eyes, and complaints of decreased night vision. A slight leucopenia was present in some workers, possibly related to the presence of benzene in the plant. Katz (*33*) showed a high prevalence of liver and hematological changes in a synthetic rubber manufacturing plant.

Zielhuis (*3*) in reviewing the literature in 1962, stated that irritation of mucosa and nonspecific asthenia and lassitude were commonly found associated with industrial exposures to styrene. Hematological abnormalities were in

Table 3. Sex and age distribution of styrene workers.

	Distribution	
Age	Number	%
<21	3	0.6
21–30	104	21.1
31–40	118	23.9
41–50	82	16.6
51–60	107	21.7
61–70	61	12.3
71+	15	3.0
Unknown	4	0.8
Total	494	100.0
Sex		
Male	485	98.2
Female	9	1.8
Total	494	100.0

general not present or were minimal. He notes that Eastern European authors regard the toxicity of styrene as serious, finding abnormalities in the central nervous system, hematological system, and liver. Zlobina in 1971 (*34*) reflected this continuing concern over low styrene concentrations.

Current Investigation

A styrene monomer and polymerization plant was studied, in which a large number of workers had had relatively pure styrene exposure for many years. This paper reports initial clinical findings in 494 workers. An investigation of the mortality experience of 563 long-term styrene workers is also currently underway.

The plant began in 1943 as a production facility for butadiene and styrene (see Fig. 1),

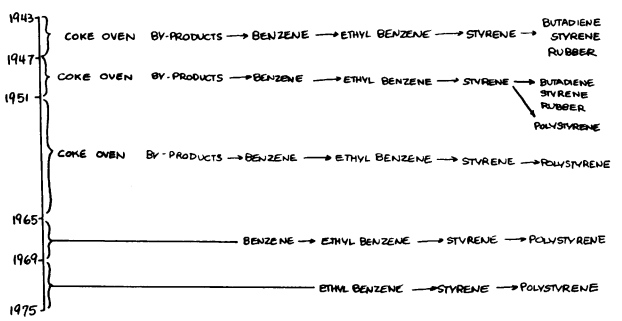


FIGURE 1. Plant history.

manufacturing the monomers but not copolymerizing them. Butadiene was produced until about 1950. Styrene and butadiene were polymerized elsewhere into butadiene rubber. Since the 1950's the principal product has been polystyrene. Limited extrusion of polystyrene also is undertaken; the remainder of the polystyrene is extruded elsewhere. Over 90% of the polystyrene coffee cups in the United States comes from polystyrene manufactured in this plant. Since 1969 ethylbenzene has been the starting product. Little benzene has been present and that in specific areas, notably the benzene building and styrene monomer purification areas (see Fig. 2). Significantly less benzene exposure occurred during the 1963–1975 period. Some toluene is recovered, primarily as a side

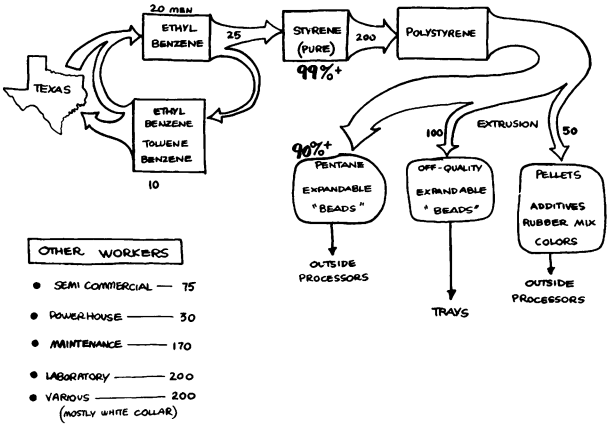


FIGURE 2. Current styrene production.

product of the ethylbenzene-styrene conversion process. About 650 workers are employed in production. Approximate numbers employed in each area are noted in Figure 2, e.g., about 20 workers are involved in storage of ethylbenzene, 200 in conversion of 99% + pure styrene to polystyrene. Most of the end product is polystyrene beads (polystyrene impregnated with various pentanes). When the "beads" are heated and extruded, they expand to polystyrene foam used for coffee cups and other articles. Off-quality beads are processed at the plant to foam trays, used primarily in the retail packaging of meat.

Characteristics of Group

The group examined numbered 494. The median age was in the 40's, but because of hiring practices in the past, the distribution is bimodal (see Table 3). Males constituted 98% of the group. Table 4 shows in which year each of the workers was first employed. Relatively few workers were first employed in the late 1950's and early 1960's.

Table 4. Year of first exposure of styrene workers.

Year	Distribution	
	Number	%
<1950	112	22.7
1950–54	94	19.0
1955–59	25	5.1
1960–64	7	1.4
1965–69	109	22.1
1970+	147	29.8
Total	494	100.0

Table 5. Information gathered.

Test information	Proportion done; selection	Purpose	Organ system
Basic demographic data (age, sex, height, weight)	All	Standardization of tests, particularly pulmonary function	
Blood chemistries (25)	All	Routine screen; special emphasis on liver	Liver
CEA	All	To select these with higher possibility for developing carcinoma	Lung, liver, other malignancy
Styrene	All	Test system for detection of styrene in low blood concentration; possible validation of occupational history categories	
Urine, protein, glucose	All	Routine screen	Kidney, endocrine
Urine, mandelic, phenylglyoxidic, and hippuric acid	All	Styrene metabolites, test of methology; possible validation of occupational history categories	
Sputum, cytology	All smokers plus nonsmokers over 40	Screen for increased atypia and malignancy	Lung
Occupational history (complete lifetime history up to last shift worked)	All	Determine specific exposure; last shift history to be related to urine metabolite levels	
Medical history	All	Elimination of effects caused by known medical conditions	
Respiratory history, standard questionnaire	All	Enables other variables to be controlled for cigarette smoking	Cardiopulmonary
Special questionnaire, acute symptoms	All	Possible acute symptoms related to styrene-irritative, prenarcotic	Eye, ENT, respiratory CNS
Physical examination	All	Chest, abdomen, peripheral nervous system especially	Nervous system, liver, spleen, pulmonary, ENT
Ophthalmological examination	All	Screening exam; external examination	Eye
Chest x-ray	All	General screen; ILO U/C pneumoconiosis reading	Lung, heart
Spirometry	All	FEV, FVC, flow at 25% of volume, FEF (25–75%)	Lung
Codiffusion	60 unselected	CO diffusing capacity, single breath	Lung
Reaction time	Unselected	Simple reaction time	Nervous system
Nerve conduction velocity	100 selected	Multiple conductions, lower and upper extremities	Peripheral nervous system
Fat aspiration	25 selected	Fat level of styrene, ethylbenzene, toluene	
Hemogram, platelets	All	See if abnormality relates to benzene or styrene areas	Hematological
Urine, mutagenic	30 selected	Possible effect on genetic material	DNA
Chromosome morphology	10 selected	Possible effect on genetic material	DNA

Studies Undertaken

Table 5 summarizes the information gathered during this examination. Selection was governed by trying to achieve clinical breadth while also trying to test hypotheses gleaned from literature review and from interviewing workers and management personnel prior to the examination. It is evident that the scientific emphasis of this survey was upon hypothesis development rather than hypothesis testing.

This report will deal with prevalence of certain symptoms (prenarcosis, acute irritation, those of chronic bronchitis) and test results (simple spirometry, chest x-ray, serum liver enzymes, hemogram, and platelet count). The above parameters will be related to estimated styrene exposure.

From review of job descriptions and actual tasks performed by those in each job, an estimate of relative exposure was obtained (see Table 6). In developing this estimate, we utilized the experience of management and of workers and had available a NIOSH Health Hazard Evaluation (*35*) of the facility. Of the 488 production and maintenance members for which adequate occupational histories are available, 200 were judged currently to be in low exposure, and 288 in relatively high styrene exposure. Significant benzene exposure was thought to be a possibility in certain job categories, as marked. Analysis is by relative exposure and time. High exposure is defined as 80% or more of years having been spent in a high exposure job. The level of 90% has been used as the dividing line for history of acute symptoms.

Table 6. Occupational distribution of high and low styrene exposure.

	Distribution, no.
Low exposure (total 200)	
Retired or working elsewhere	41
Power house	22
Handling of extruded polystyrene or finished beads	
Sheet plant	41
Polystyrene handler	16
Packaging operator	25
Handling and transportation, miscellaneous packaged materials	22
Maintenance, low exposure	22
Other	11
High exposure (total 288)	
Production:	
Styrene manufacture	16
Styrene purification [a]	14
Styrene polymerization	
To polystyrene	70
To copolymers, special processes [a]	38
Miscellaneous production workers [a]	25
Polystyrene extrusion	14
Maintenance:	
Pipe fitters [a]	29
Millwrights [a]	19
Electrician	15
Laborer	13
Welder	11
Other	20
Other high exposure [a]	4

[a] Significant benzene exposure possible.

Results

Styrene at high concentrations (hundreds of ppm) produces a prenarcotic syndrome, described by the individual affected as being "lightheaded" or "drunk." An attempt was made to exclude prenarcosis due to other substances (such as pentane) which also cause the syndrome. Of the workers 13% overall had had at least one episode of prenarcosis (see Table 7). Those with high styrene exposure had significantly more prenarcosis than those with low exposure.

Table 7. Acute prenarcotic symptoms in styrene-exposed workers.

Styrene exposure	History of prenarcotic symptoms [a] 0.1–7.0 yr	7.1–20 yr	>20.0 yr	Total
Low	15/143 (10%)	2/61 (3.3%)	13/102 (13%)	30/306 (10%)
High	3/34 (9%)	11/53 (21%)	20/95 (21%)	34/182 (19%)
Total	18/177 (10%)	13/144 (11%)	33/197 (17%)	64/488 (13%)

[a] Significance for high as compared with low: $\chi^2 = 7.81$, $0.001 < p < 0.01$; $\chi^2 = 0.08$, NS (0.1–7.0 yr); $\chi^2 = 8.57$, $0.001 < p < 0.01$ (7.0–20.0 yr); $\chi^2 = 2.43$, NS (>20.0 yr).

Acute mucous membrane irritation is a common occurrence above levels of 50–100 ppm in experimental work with subjects never before exposed to styrene. Significant tolerance may develop in industrial populations. This fact may explain our failure to find differences in prevalence between relatively high and low styrene (see Table 8).

The workers were also asked if they ever had wheezing or tightness in the chest from styrene vapors. In this case 11% of workers had such an episode. Significantly more high than low exposed workers had had this symptom (see Table 9).

Table 8. Mucous membrane irritation in styrene-exposed workers.

Styrene exposure	History of mucous membrane irritation 0.1–7.0 yr	7.1–20 yr	>20.0 yr	Total
Low	28/143 (20%)	6/61 (10%)	17/102 (17%)	51/306 (17%)
High	4/34 (12%)	11/53 (21%)	22/95 (23%)	37/182 (20%)
Total	32/177 (18%)	17/114 (15%)	39/197 (20%)	88/488 (18%)

Table 9. Acute lower respiratory symptoms in styrene-exposed workers.

Styrene exposure	History of acute lower respiratory symptoms [a] 0.1–7.0 yr	7.1–20 yr	>20.0 yr	Total
Low	9/143 (6.3%)	5/61 (8%)	8/102 (8%)	22/306 (7.2%)
High	4/34 (12%)	13/53 (25%)	17/95 (18%)	34/182 (19%)
Total	13/177 (7%)	18/114 (16%)	25/197 (13%)	56/488 (11%)

[a] Significance for low compared with high: $\chi^2 = 14.84$, $p < 0.001$ (overall); $\chi^2 = 1.21$ NS (0.1–7 yr); $\chi^2 = 5.69$, $0.01 < p < 0.02$ (7.1–20.0 yr); $\chi^2 = 4.49$, $0.02 < p < 0.05$ (>20.0 yr).

The same pattern is present for recurrent symptoms, i.e., present weekly to monthly over a period of time (see Table 10); 12.1% of the workers in the high styrene area versus 4.9% of those in low-styrene exposures had recurrent episodes.

Table 10. Recurrent acute lower respiratory symptoms in styrene-exposed workers.

Styrene exposure	History of recurrent lower respiratory symptoms [a] 0.1–7.0 yr	7.1–20 yr	>20.0 yr	Total
Low	6/143 (4.2%)	3/61 (4.9%)	6/102 (5.9%)	15/306 (4.9%)
High	2/34 (5.9%)	8/53 (15%)	12/95 (13%)	22/182 (12.1%)
Total	8/177 (4.5%)	11/114 (9.6%)	18/197 (9.1%)	37/488 (7.6%)

[a] Significance for low styrene exposure as compared with high styrene exposure: $\chi^2 = 8.41$, $0.001 < p < 0.01$.

The prevalence of chronic bronchitis was investigated (see Table 11); 19% of the workers reported such symptoms.

Table 11. Chronic bronchitis in styrene-exposed workers.

Styrene exposure	Prevalence of chronic bronchitis [a] 0.1–7.0 yr	7.1–20 yr	>20.0 yr	Total
Low	6/83 (7.2%)	7/61 (11%)	22/78 (28%)	35/222 (16%)
High	9/61 (15%)	17/70 (24%)	28/119 (24%)	54/250 (22%)
Total	15/144 (10%)	24/131 (18%)	50/197 (25%)	89/472 (19%)

[a] Definition: cough and sputum production on most days for at least 3 months for at least 2 yr.

To eliminate the effect of smoking, nonsmokers were analyzed separately (see Table 12). Of the nonsmokers, 6% had symptoms consistent with chronic bronchitis. No trends were noted. We have seen such findings in other industrial populations. It is questionable whether styrene exposure had etiological importance in this population.

Table 12. Chronic bronchitis in nonsmoking styrene-exposed-workers.

Styrene exposure	Prevalence of chronic bronchitis in nonsmokers [a] 0.1–7.0 yr	7.1–20 yr	>20.0 yr	Total
Low	2/19 (11%)	2/18 (11%)	0/13 (0%)	4/50 (8%)
High	1/15 (7%)	0/15 (0%)	0/23 (0%)	1/53 (2%)
Total	3/34 (9%)	2/33 (6%)	0/36 (0%)	5/103 (5%)

[a] Definition: cough and sputum production on most days for at least 3 months for at least 2 years.

The prevalence of airway obstruction defined as $FEV_1/FVC < 75\%$ was also investigated (see Table 13). Overall, 35.3% satisfied this criteria for obstruction; here, the high and low styrene groups were statistically different. Of the nonsmokers, 31.6% had evidence of airways obstruction (see Table 14), although no

pattern consistent with a simple dose-response relationship was present. As expected, obstruction increased with years on the job among smokers (see Table 15). Overall, 5.9% of the men had FVC < 80% predicted (see Table 16); restriction was not of significance in this group of workers.

Table 13. Airway obstruction ($FEV_1/FVC < 75\%$) in styrene-exposed workers.[a]

Styrene exposure	Prevalence of airway obstruction[b] 0.1–7.0 yr	7.1–20 yr	>20.0 yr	Total
Low	17/82 (21%)	18/60 (30%)	36/72 (50%)	71/214 (33%)
High	15/60 (25%)	27/69 (39%)	50/108 (46%)	92/237 (39%)
Total	32/142 (23%)	45/129 (35%)	86/180 (46%)	163/451 (35.2%)

[a] FEV-forced expiratory volume at 1 sec; FVC-forced vital capacity.

[b] Significance for low styrene exposure as compared with high styrene exposure: $\chi^2 = 2.17$, not significant (NS).

Table 14. Airway obstruction ($FEV_1/FVC < 75\%$) in nonsmoking styrene-exposed workers.

Styrene exposure	Prevalence of airway obstruction[a] 0.1–7.0 yr	7.1–20 yr	>20.0 yr	Total
Low	5/19 (26%)	6/18 (33%)	7/13 (54%)	18/50 (36%)
High	5/15 (33%)	3/15 (20%)	5/23 (22%)	13/53 (25%)
Total	10/34 (29%)	9/33 (27%)	12/36 (33%)	31/103 (30%)

[a] Significance for low styrene exposure as compared with high styrene exposure: $\chi^2 = 1.46$ (NS).

Table 15. Airway obstruction ($FEV_1/FVC < 75\%$) in smoking styrene-exposed workers.

Styrene exposure	Prevalence of airway obstruction[a] 0.1–7.0 yr	7.1–20 yr	>20.0 yr	Total
Low	8/49 (16%)	10/29 (34%)	21/34 (62%)	39/112 (35%)
High	8/40 (20%)	17/43 (40%)	21/41 (51%)	46/124 (37%)
Total	16/89 (18%)	27/72 (38%)	42/75 (56%)	85/236 (36%)

[a] Significance for low styrene exposure as compared with high styrene exposure: $\chi^2 = 0.13$ (NS).

Table 16. Restriction (FVC < 80% predicted) in styrene-exposed workers.

Styrene exposure	Prevalence of restriction 0.1–7.0 yr	7.1–20 yr	>20.0 yr	Total
Low	3/82 (3.7%)	4/60 (6.7%)	5/72 (6.9%)	12/214 (5.6%)
High	1/60 (1.7%)	1/69 (1.4%)	5/108 (4.6%)	7/237 (2.9%)
Total	4/142 (2.8%)	5/129 (3.9%)	10/180 (5.6%)	19/451 (4.2%)

The x-rays were categorized by the ILO-U/C International Classification of Radiographs of Pneumoconiosis (see Table 17). Apart from those with history of previous coal or asbestos exposure there was no finding of significant radiological change; surely not at the level we have seen in vinyl chloride workers (*31*).

Table 17. Abnormal x-ray findings among styrene-exposed workers.[a]

Styrene exposure	ILO U/C classification 1/0–1/2	2/1–2/3	3/2–3/4	Total
Low	17/250 (6.8%)	5/250 (2.0%)	1/250 (0.4%)	23/250 (9.2%)
High	14/167 (8.4%)	4/167 (2.4%)	0/167 (0%)	18/167 (11%)
Total	31/417 (7.4%)	9/417 (2.2%)	1/417 (0.21%)	41/417 (9.8%)

[a] Excluding those with known prior exposure to asbestos or coal dust.

Hepatic function was investigated by using bilirubin, alkaline phosphatase, SGPT, GGTP, and SGOT as parameters (see Table 18). The distribution of the abnormal results was investigated. For this initial analysis, "abnormal" was defined as at or above the 96th percentile as compared with a group of 993 nonhospitalized men aged 40–44 tested at the same laboratory; 471 sets of results were available for analysis.

When tested for styrene (high and low) and duration, only GGTP showed a nonrandom pattern (see Table 19). Overall, 4.9% were elevated: 6.7% in the high styrene and 2.8% in the low styrene groups. This difference was statistically significant. The difference shown

Table 18. Liver function tests on 471 styrene-exposed workers.

	"Positives"[a]	
	No.	%
Bilirubin ≧ 1.0 mg %	15	3.2%
Alkaline phosphatase ≧ 41 units	28	5.9%
SGPT ≧ 70 I.U.	19	4.0%
GGTP ≧ 45 I.U.	23	4.9%
SGOT ≧ 50 I.U.	16	3.4%

[a] Defined as 96th percentile or higher as compared with a group of 993 nonhospitalized men aged 40–44, done at same laboratory.

in the > 20 and < 20 yr groups is significant but needs to be adjusted for age-dependent increase in GGTP. When those with alcohol consumptions of more than 400 proof ounces (2 oz pure ethanol) per week are excluded (see Table 20), the differences increase between the low and high styrene groups. For those currently working, those with low styrene and high styrene with concurrent relatively low and high benzene are compared (see Table 21). No comparisons reach statistical significance, although both chemicals may have an effect on the prevalence of GGTP. No other patterns were observed when we analyzed other liver function tests in a similar manner.

Table 19. Elevated GGTP in styrene-exposed workers.

	Incidence of elevated GGTP[a]			
Styrene exposure	0.1–7.0 yr	7.1–20 yr	>20.0 yr	Total
Low	1/83 (1.2%)	1/60 (1.7%)	4/75 (5.3%)	6/218 (2.8%)
High	1/62 (1.6%)	2/72 (2.8%)	14/119 (12%)	17/253 (6.7%)
Total	2/145 (1.4%)	3/132 (2.3%)	18/194 (9.3%)	23/471 (4.9%)

[a] Significance for high styrene compared with low styrene: $\chi^2 = 3.93$, $0.02 < p$ 0.05; for over 20 yr compared with under 20 yr: $\chi^2 = 13.72$, $p < 0.001$.

Hematological parameters investigated included hemoglobin, white blood count, and platelet count (see Table 22): 13.6% of the workers had hemoglobin levels below 14.0 g-%; 2.7% had white blood counts below 4800; and 7.4% had platelet counts below 180,000. Analyses similar to that performed on the liver function results showed random distribution of the abnormalities.

Table 20. Elevated GGTP in styrene exposed workers with low alcohol intake.[a]

	Incidence of elevated GGTP[b]			
Styrene exposure	0.1–7.0 yr	7.1–20 yr	>20.0 yr	Total
Low	0/68 (0%)	1/53 (1.9%)	2/56 (3.6%)	3/177 (1.7%)
High	1/52 (1.9%)	2/60 (3.3%)	12/96 (13%)	15/208 (7.2%)
Total	1/120 (0.8%)	3/113 (2.7%)	14/152 (9.2%)	18/385 (4.7%)

[a] Workers consuming ≧400 proof ounces/week alcohol excluded.

[b] Significance for high styrene compared with low styrene: $\chi^2 = 6.53$, $0.01 < p < 0.02$; for over 20 yr compared with under 20 yr: $\chi^2 = 11.59$, $p < 0.001$.

Table 21. Elevated GGTP of styrene-exposed workers currently working.[a]

	Incidence of elevated GGTP[b]		
Styrene exposure	Low benzene exposure	High benzene exposure	Total
Low	4/161 (2.5%)	—	4/161 (2.5%)
High	7/132 (5.3%)	6/109 (5.5%)	13/241 (5.4%)
Total	11/293 (3.8%)	6/109 (5.5%)	17/402 (4.2%)

[a] Workers consuming ≧400 proof ounces/week alcohol excluded.

[b] No significant differences.

Over 300 fundal examinations were made by an opthalmologist. No optic neuritis or other unexplained fundal abnormalities were noted. A case report (*28*) of possible association between styrene and optic neuritis has been published. Analysis of the remaining tests will be reported later.

Table 22. Hematological parameters in styrene-exposed workers.

	Positive	
Parameter	No.	%
Hemoglobin <14.0 g-%	66/486	13.6
White blood count <4800	13/486	2.7
Platelet count <180,000	36/486	7.4

Discussion

The results of this clinical survey confirm styrene to be an irritant of the mucous membranes of the upper respiratory tract. The possibility that styrene may also be a significant lower respiratory irritant in occupational groups must also be considered. That 30% of the nonsmokers had $FEV_1/FVC < 75\%$, and that 12% of the high exposed workers (compared to 4% of the lower exposed) had repeated episodes of wheezing and/or tightness in the chest suggests an etiological relationship.

Serum γ-glutanyl transpeptidase was higher among those with higher exposure, consistent with hepatic changes. Hematological findings did not yield evidence of significant marrow depression in this preliminary analysis.

In comparison with findings of studies (*36, 37*) done in a similar manner of workers exposed to another monomer, vinyl chloride, there was no evidence of characteristic vinyl chloride monomer changes such as Reynaud's syndrome, acroosteolysis, clinical hepatic disfunction, or skin changes No overt neoplasms were found in this survey.

Summary

Initial analysis of findings in a clinical survey of 494 workers at a styrene manufacturing, polymerization, and polystyrene extrusion facility has been undertaken. No unusual clinical patterns emerged, although styrene monomer is confirmed as an irritant and CNS depressant, and some changes in pulmonary function and in serum GGTP were found. An investigation of the mortality experience of workers at this facility is underway and will be reported later, as will findings of other studies performed during this survey of styrene-exposed workers.

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